

Rates of amine substitution reactions in methanol and *n*-hexane solvents at 25°

Pt ^{II} complex	Reagent	10 ⁵ <i>k_a</i> (sec. ⁻¹) ^a	10 ⁵ <i>k_y</i> (M ⁻¹ sec. ⁻¹) ^a	Ratio <i>k_a</i> ^a	10 ⁴ <i>k_y</i> (M ⁻¹ sec. ⁻¹) ^b	Ratio <i>k_y</i> ^b	<i>E_{act}</i> (kcal./mole) ^d	log <i>A</i> ^{b,d}
Pr ⁿ ₃ P, PtCl ₂ NHET ₂	Et ₂ NH ^c	0.86	0	1.0	1.4	1.0	15.2 ± 0.3	6.35
Et ₂ P, PtCl ₂ NHET ₂	Et ₂ NH ^c	1.01	0	1.25	2.1	1.5		
Me ₃ P, PtCl ₂ NHET ₂	Et ₂ NH ^c	1.69	0	0.1	3.6	2.5	15.0 ± 0.3	6.65
Pr ⁿ ₃ P, PtCl ₂ NHMe ₂	Et ₂ NH	13.5	7.5	15.7	85	60.5	14.3 ± 0.3	7.45
Pr ⁿ ₃ P, PtCl ₂ NHET ₂	Me ₂ NH	0.86	4	1.0	66	47		
Pr ⁿ ₃ P, PtI ₂ NHET ₂	Et ₂ NH	0.52	0	0.65	0.4	0.27	15.5 ± 0.3	6.00
Pr ⁿ ₃ P, PtI ₂ NHMe ₂	Et ₂ NH	10.8	2.5	12.8	23			

^a Methanol results; ^b *n*-hexane results; ^c *k_a*, *k_y* values from data reported graphically in ref. 5; ^d log *A* values from rates measured at 25° for complex concentration of 5 × 10⁻³M and reagent concentration of 0.1M.

shorter amine hydrocarbon chains is seen, from Δ*E_{act}* and log *A* values in the Table, to be due to a comparatively small activation-energy change (rate factor of 4) and a larger change in frequency factor (rate factor of 15). This data is consistent with the view that this acceleration is due largely to the removal of steric hindrance.

We also note that rates (*k_y* values) of direct substitution of co-ordinated Et₂NH by Me₂NH are similar to those for

the reverse reaction, which further supports the postulate of the formation of a trigonal bipyramidal transition state, in which it is considered that in this configuration the entering and leaving amine groups occupy similar positions.¹

The expected small *cis*-effects are observed in the cases of isomeric di-iodo-complexes.

(Received, November 26th, 1968; Com. 1617.)

- ¹ F. Basolo, "Mechanisms of Inorganic Reactions", ed. R. F. Gould, Advances in Chemistry Series, A.C.S., 1965, No. 49, ch. 4.
² C. H. Langford and H. B. Gray, "Ligand Substitution Reactions", W. A. Benjamin, New York, 1965, ch. 2.
³ R. D. Cramer, R. V. Lindsey, C. T. Prewitt, and U. G. Stolberg, *J. Amer. Chem. Soc.*, 1965, 87, 658; G. A. Mair, H. M. Powell, and L. M. Venanzi, *Proc. Chem. Soc.*, 1961, 170.
⁴ F. Basolo, J. Chatt, H. B. Gray, R. G. Pearson, and B. L. Shaw, *J. Chem. Soc.*, 1961, 2207.
⁵ A. L. Odell and H. A. Raethel, *Chem. Comm.*, 1968, 1323.
⁶ T. P. Cheeseman, A. L. Odell, and H. A. Raethel, *Chem. Comm.*, 1968, 1496.

The Total Synthesis of (±)-Ibogamine

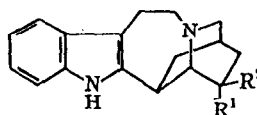
By MUNEYOSHI IKEZAKI, TAKESHI WAKAMATSU, and YOSHIO BAN*

(Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan)

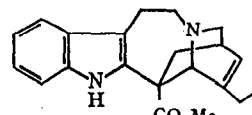
(±)-IBOGAMINE (Ia) was synthesized independently by Büchi,¹ Kutney,² Nagata,³ and Sallay.⁴ We also reported the synthesis of (±)-epi-ibogamine (Ib),⁵ and recently the biogenetic-type synthesis of (±)-catharanthine (II) has been achieved by Scott.⁶ We have now extended our method to the synthesis of (±)-ibogamine(Ia), which involves separation of the stereoisomers of the penultimate products (VI).

The Ziegler cyclization of (III),⁵ obtained in four stages from 3-cyanopyridine, gave a complicated mixture of products, which was separated by silica gel chromatography to give two enamines: (IVa) m.p. 163–164° (recrystallized from ethyl acetate), i.r. (Nujol) 2240, 2180 cm.⁻¹, in 37% yield; and (IVb) m.p. 240–246° (recrystallized from ethyl acetate), i.r. (Nujol) 2225(w), 2170(s) cm.⁻¹, in 10% yield.

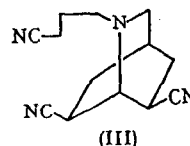
The enamine (IVa) was hydrolysed with concentrated hydrochloric acid, and the product esterified with diazo-methane to afford the ketone (Va), m.p. 74°, recrystallized from *n*-hexane. The acetal-ester (Vb) obtained from the above ketone (Va), was converted by Corey's method into the methanesulphonyl derivative (Vc),⁷ which without isolation was reduced with aluminium amalgam to (Vd), which was an oil, giving two spots on t.l.c. This oil, without purification, was subjected to the Huang-Minlon reduction, giving (Ve). Subsequent acidic hydrolysis gave the ketone (VI) as an oil, which was purified by chromatography on silica gel. Elution with ethyl acetate afforded the (VIa) as an oil, i.r. (film) 1700 cm.⁻¹; n.m.r. (CDCl₃) τ 9.08(3H, t, *J* 6 c./sec.); picrate, m.p. 178–180°. The other fraction eluted with ethyl acetate and successively with methyl chloride: ethanol (9:1) yielded (VIb) as an oil, i.r. (film) 1700 cm.⁻¹; n.m.r. (CDCl₃) τ 9.08(3H, t, *J* 6



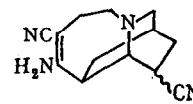
(Ia); R¹=H, R²=Et
b; R¹=Et, R²=H



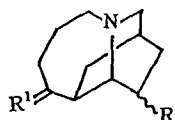
(II)



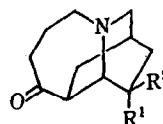
(III)



(IV a, b)



(V) a R¹ O, R² CO₂Me
b O[CH₂]₂O, CO₂Me
c O[CH₂]₂O, CO-CH₂-SO₂-Me
d O[CH₂]₂O, CO-Me
e O[CH₂]₂O, Et



(VI)a; R¹=H, R²=Et
b; R¹=Et, R²=H

c./sec.); picrate, m.p. 184–186°. The ratio of (VIa) and (VIb) was approximately 2:3, and each gave one spot on

t.l.c. The R_F value of (VIa) was slightly greater than that of (VIb), suggesting that the former is the *exo*-ethyl ketone (VIa) and the latter the *endo*-ethyl derivative (VIb).

A mixture of (VIa) and phenylhydrazine in ethanol was heated at reflux for 6 hr., and to the resulting mixture was added anhydrous formic acid.⁸ The whole solution was heated at 100° in a current of nitrogen for 30 min. to afford ($\pm$)-ibogamine, m.p. 132–134° (recrystallized from diisopropyl ether) in 48% yield, identified by mixed m.p.,

i.r., u.v., mass spectroscopic, and t.l.c. comparison with the authentic specimen kindly supplied by Dr. W. Nagata.

On treatment of (VIb) in a similar way, ($\pm$)-epi-ibogamine (Ib), m.p. 194–196°, was obtained in 60% yield.

We thank the United States Public Health Service, National Institutes of Health, for support.

(Received, November 28th, 1968; Com. 1630.)

¹G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Amer. Chem. Soc.*, 1965, **87**, 2073; 1966, **88**, 3099.

²J. P. Kutney, W. J. Cretney, P. Le Quesne, B. McKague, and E. Piers, *J. Amer. Chem. Soc.*, 1966, **88**, 4756.

³W. Nagata, S. Hirai, K. Kawata, and T. Okumura, "The Text of the 11th Symposium on the Chemistry of Natural Products held in Kyoto, Japan," 1967, p. 41. Cf. W. Nagata, S. Hirai, K. Kawata, T. Okumura, *J. Amer. Chem. Soc.*, 1967, **89**, 5046.

⁴S. I. Sallay, *J. Amer. Chem. Soc.*, 1967, **89**, 6762.

⁵Y. Ban, T. Wakamatsu, Y. Fujimoto, and T. Oishi, *Tetrahedron Letters*, 1968, 3383; Cf. Y. Ban, T. Oishi, M. Ochiai, T. Wakamatsu, and Y. Fujimoto, *ibid.*, 1966, 6385.

⁶A. A. Qureshi and A. I. Scott, *Chem. Comm.*, 1968, 947.

⁷E. J. Corey and M. Chaykowsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1347.

⁸Y. Ban, T. Oishi, Y. Kishio, and I. Iijima, *Chem. and Pharm. Bull. (Japan)*, 1967, **15**, 531.

Reaction of Methylene cyclopropanes with Enneacarbonyl di-iron: a New Route Tricarbonyltrimethylenemethaneiron Complexes

By R. NOYORI,* T. NISHIMURA, and H. TAKAYA

(Department of Chemistry, Nagoya University, Chikusa-Ku, Nagoya, Japan)

STABILIZATION of unstable organic molecules, including cyclobutadiene,¹ carbene,² *o*-quinodimethane,³ and benzyne⁴ as transition-metal ligands has been studied. Trimethylenemethane (I) has also received attention because of the maximum bond order possible for the central carbon atom,⁵ and the triplet ground electronic state.⁶ The stabilisation of the reactive species as the tricarbonyliron complex (IIa) was first achieved by reduction of 3-chloro-(2-chloromethyl)-propene with enneacarbonyl di-iron.⁷ We report a convenient synthesis of tricarbonyliron complexes of substituted trimethylenemethanes, from readily accessible methylenecyclopropane derivatives (III).⁸

An equimolar mixture of 1-methylene-2-phenylcyclopropane (IIIb) and enneacarbonyl di-iron in benzene was stirred at room temperature for 5 hr. under nitrogen to give tricarbonyl(phenyltrimethylenemethane)iron (IIb) (40%). The structure was confirmed by comparison of the i.r. and n.m.r. spectra with those of an authentic specimen. Similarly 2-methyl-2-phenyl- and 2,2-diphenyl-methylenecyclopropane [(IIIc) and (IIId)] gave (IIc) (60%) and (IIId) (60%). Methylenecyclopropane (IIIa) itself, however, gave butadienetricarbonyliron (ca. 2%) rather than (IIa). As might be expected, the mass spectra of the trimethylenemethane complexes (IIb–d) exhibited characteristic cracking patterns arising from successive loss of carbon monoxide, and other fragmentations showed close resemblance to those of the original methylenecyclopropanes.

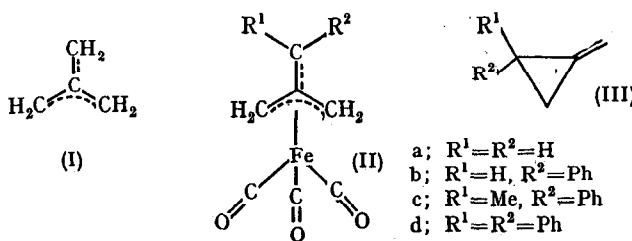
Introduction of phenyl groups into the trimethylenemethane portion of the complex does not greatly affect the

principal carbonyl frequencies (Table).⁹ This might imply that, in agreement with the result of the X-ray diffraction study,¹⁰ the phenyl ring is not coplanar with the plane of the adjacent sp^2 carbon atom even in solution.

Tricarbonyl(trimethylenemethane)iron complexes

	M.p.	vco (cm. ⁻¹ (in CCl ₄))*	
		Narrow band	Broad band
(IIa)	32.5–33.0°	2061m	1995s, 1966w
(IIb)	63–64	2058m	1990s, 1966w
(IIc)	Oil	2087w, 2054m, 2010m	1993s, 1960w
(IIId)	157–158	2057m	1995s, 1965w

* The values are believed to be accurate to ± 1 cm.⁻¹.



We thank Professor M. R. Churchill, Harvard University, for identification of the complex (IIb).

(Received, December 3rd, 1968; Com. 1653.)

¹G. F. Emerson, L. Watts, and R. Pettit, *J. Amer. Chem. Soc.*, 1965, **87**, 131.

²E. O. Fischer and A. Maasböl, *Chem. Ber.*, 1967, **100**, 2445.

³W. R. Roth and J. D. Meier, *Tetrahedron Letters*, 1967, 2053.

⁴E. W. Gwilling, S. F. A. Kettle, and G. M. Sharples, *Chem. Comm.*, 1968, 21.

⁵J. D. Roberts, "Notes on Molecular Orbital Calculations," Benjamin, New York, 1961, p. 56.

⁶P. Dowd, A. Gold, and K. Sachdev, *J. Amer. Chem. Soc.*, 1968, **90**, 2715.

⁷G. F. Emerson, K. Ehrlich, W. P. Giering, and P. C. Lauterber, *J. Amer. Chem. Soc.*, 1966, **88**, 3172.

⁸R. Noyori, H. Takaya, Y. Nakanishi, and H. Nozaki, *Canad. J. Chem.*, in the press.

⁹R. Pettit and G. F. Emerson, *Adv. Organometallic Chem.*, 1964, **1**, 10.

¹⁰M. R. Churchill and K. Gold, *Chem. Comm.*, 1968, 693.